

PATENT CLAIMS

1. A method for fluorescence analysis comprising illuminating a granular composition comprising a purified biologically active compound with light capable of fluorescence excitation of a
5 fluorescent marker comprised in the granular composition, detecting light emitted from the fluorescent marker and predicting the amount of fluorescent marker in the granular composition accessible to fluorescence excitation.
- 10 2. The method of claim 1, wherein the granular composition is illuminated with a light source producing ultraviolet light having wavelengths between 10-380 nm.
3. The method of claim 2, wherein the ultraviolet light consist
15 of 1-10 discrete monochromatic wavelengths.
4. The method of claim 3, wherein the ultraviolet light consist of one discrete monochromatic wavelength, particularly between
20 260-280 nm.
5. The method of claim 1, wherein the detecting of light emitted from the fluorescent marker consists of detecting emitted light of 1-10 discrete monochromatic wavelengths, particularly between
25 185-2600 nm.
6. The method of claim 5, wherein the fluorescent marker is the biologically active compound and the detecting of light emitted from the fluorescent marker consists of detecting emitted light
30 300-400 nm.

7. The method of claim 1, wherein the detecting is made with at least one detector capable of converting the emitted light into an electronic signal.

5 8. The method of claim 7, wherein the detecting is made with a CCD or an ICCD camera capable of converting the emitted light into a digital two-dimensional image.

9. The method of claim 8, wherein the detecting is made with at
10 least two CCD or ICCD cameras capable of converting the emitted light into a digital two dimensional image.

10. The method of claim 1, wherein the prediction is conducted by comparison of light emitted from the particulate composition
15 with light emitted from a particulate composition with known amounts of fluorescent marker.

11. The method of claim 10, wherein the prediction is made in real time.

12. The method of claim 1, wherein the biologically active compound is selected from bio-catalysts, therapeutic agents, herbicides, pesticides and fungicides.

25 13. The method of claim 12, wherein the biologically active compound is selected from proteins and peptides.

14. The method of claim 13, wherein the biologically active compound is an enzyme, particularly a selected from hydrolases
30 and oxidoreductases.

15. The method of claim 1, wherein the granular composition further comprises auxiliary granulation agents.

16. The method of claim 15, wherein the auxiliary granulation agents are selected from fiber materials, binders, fillers, liquid agents, enzyme stabilizers, suspension agents, cross linking agents, mediators and/or solvents

17. The method of claim 16, wherein the fluorescent marker is an auxiliary granulation agent and the detecting of light emitted from the fluorescent marker consists of detecting emitted light of one discrete monochromatic wavelength, particularly between 350-500 nm.

18. The method of claim 1, wherein the granules comprises a core wherein the biologically active compound is intimately mixed with auxiliary granulation agents.

19. The method of claim 1, wherein the granules comprise a core particle coated with a layer comprising the biologically active compound and particularly auxiliary granulation agents.

20. The method of claim 1, wherein the granules have an average size between 20-2000 μm , particularly between 100-1000 μm , more particularly between 200-800 μm .

21. The method of claim 1, wherein the granules are coated with a coating agent.

22. A process for preparing granules comprising a purified biologically active compound, a fluorescent marker and optionally auxiliary granulation agents in a granulation

apparatus said process comprising the step of performing fluorescence analysis on the fluorescent marker in accordance with claims 1-21 on the granules forming in the granulator.

5 23. The process of claim 22, wherein the fluorescence analysis is performed on-line and in real time during the granulation process and is repeated more than one time during the granulation process.

10 24. The process of claim 22, further comprising the step of changing at least one process parameter as a result of the fluorescence analysis.

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15 25. The process of claim 24, wherein process parameter is selected from supply of biologically active compound, supply of auxiliary granulation agent, supply of coating agent, supply of gas, temperature, pressure, pH and mechanical force conferred to the granulation material.

20 26. The process of claim 22-25, further characterized by being a coating process wherein granules comprising a biologically active compound and optionally auxiliary granulation agents are coated with a coating agent and the parameter is supply of coating agent to the granulation apparatus.

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27. The process of claim 22, wherein the fluorescence analysis is performed at-line and in real time after the granulation process and repeated more than one time.

30 28. A granulation or coating apparatus comprising

(a) a granulation or coating device comprising at least one chamber for processing material into granules or coated granules,

(b) an optical arrangement for performing fluorescence analysis comprising a light source for illumination of granules being processed, at least one detector capable of detecting light emitted from the granules being processed, means for projecting illuminating light onto a portion of the granules being processed, means for projecting light emitted from illuminated granules to the detector and at least one filtering device for filtering light.

29. The apparatus of claim 28, wherein the granulating or coating device is selected from a fluid bed granulator or coater, high shear mixer granulator, a spray dryer, a spray cooler, an extruder.

30. The apparatus of claim 28, wherein the light source is selected from a glow lamp, a xenon lamp or a stroboscope lamp, particularly capable of delivering light having wavelengths between 10-700 nm.

32. The apparatus of claim 28, wherein the detector is a camera, particularly selected from a line-scan camera, a CCD or an ICCD camera.

33. The apparatus of claim 28, wherein the means for projecting illuminating light onto the granules being processed and projecting emitted light from said granules to the detector is selected from one or more of fiber optics, mirrors, lenses and beam splitters.

34. The apparatus of claim 28, wherein the filtering device is positioned so than only the emitted light is filtered and so that the emitted light must pass the filter before reaching the detector.

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35. The apparatus of claim 34, wherein at least two filtering devices are positioned so that both the illuminating light and the emitted light is filtered.

10 36. The apparatus of claim 28, wherein the optical arrangement comprises a stroboscope light source, 2 CCD camera detectors, one band pass filter for filtering illumination light, two band pass filters for filtering emitted light, a lens, a two dichroic mirror beam splitters.

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37. The apparatus of claim 28, wherein the portion of granules being processed is present in the chamber.

38. The apparatus of claim 28, further comprising means for
20 providing a purge stream of granules from the chamber and wherein the optical arrangement is positioned to allow fluorescence analysis of granules in the purge stream.

39. The apparatus of claim 38, wherein the means for providing a
25 purge stream includes means for forming a single layer of granules.

40. The apparatus of claim 39, wherein the means for forming a single layer of granules comprise a tilted vibrating surface.

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41. The apparatus of claim 40, wherein the optical arrangement is positioned so that the fluorescence analysis is performed on

a single layer of granules after falling over one or more edges of the vibrating surface.

42. The apparatus of claim 28, further comprising one or more
5 elements selected from computing units and control units

43. Use of fluorescence analysis on granules comprising a purified biologically active compound.

10 44. A method according to claim comprising the steps of:

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- 15 a) providing a calibration model by illuminating a granular composition comprising a purified biologically active compound having a known quality parameter with light capable of fluorescence excitation of a fluorescent marker comprised in the granular composition, recording one or more images of the light emitted from the granular composition of a known quality and subjecting recorded images to data processing, particularly in the form of partial least squares data processing, to form a calibration model,
- 20 b) illuminating a unknown granular composition comprising a purified biologically active compound with light capable of fluorescence excitation of a fluorescent marker comprised in the granular composition, recording at least
- 25 one image of the light emitted from the unknown granular composition,
- c) comparing at least one image of the unknown granular composition with the calibration model and
- 30 d) estimating the quality parameter of the unknown granular composition.